

<b>Notice of Allowability</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	09/691,763		VERTINO, PAULA M.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Jeanine A Goldberg		1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to November 12, 2002.
2. ☒ The allowed claim(s) is/are 1,47 and 110-124.
3. ☒ The drawings filed on 18 October 2000 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No. \_\_\_\_\_.
  - (b) ☐ including changes required by the proposed drawing correction filed \_\_\_\_\_, which has been approved by the Examiner.
  - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |   |
|---|---|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892)   | 2 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)          |
| 3 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 4 <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____.            |
| 5 <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. <u>23</u> . | 6 <input checked="" type="checkbox"/> Examiner's Amendment/Comment                  |
| 7 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material    | 8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
|   | 9 <input type="checkbox"/> Other _____  |

### **EXAMINER'S AMENDMENT**

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Maria Trevisan on December 17, 2002.

3. The application has been amended as follows:

A) Claims 5, 13, 15, 18, 21, 22, 30, 38, 58, 61, 67, 68, 71, 72, 89, 95, 101, 105 have been cancelled as drawn to non-elected subject matter.

4. The following is an examiner's statement of reasons for allowance.

The claims are drawn to methods of identifying a subject at risk of developing cancer by abnormally increased methylation of a CpG island containing TMS1 by comparing level of methylation of the CpG island with a control wherein increased methylation is indicative of increased risk of developing cancer. The claims requires a CpG island TMS1 nucleic acid molecule which both hybridizes under stringent conditions to SEQ ID NO: 4 and codes for a TMS1 polypeptide comprising a caspase recruiting domain and having apoptosis inducing activity. Moreover, the claims are drawn to methods of identifying a subject having cancer who is at risk of being non-responsive to an apoptosis-dependent anti-cancer therapy.

The prior art teaches the hypermethylation of CpG islands is indicative of increased risk for cancers (Nelson, US Patent 5,552,277; Baylin, US Patent 5,756,668;

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Herman, US Patent 5,786,146). The art, however, does not teach the hypermethylation of a CpG island containing TMS1 nucleic acid.

In addition to the breast cancer tumor sample data in the specification, the declaration filed January 18, 2002 by Paula Vertino under 1.132 illustrates that TMS1 methylation status was analyzed in additional tissue samples. The declaration provides that normal human brain tissue and primary human glioblastoma multiforme tumor samples, in addition to additional cell lines. The declaration provides that "eight out of seventeen (i.e., 47%) primary glioblastoma multiform tumor samples analyzed demonstrate TMS1 methylation. Figure 2 illustrates eleven samples considered to be representative of the seventeen" (page 2 of Declaration filed January 18, 2002).

Therefore, in view of the applicant's arguments, the declaration filed under 1.132 and the amendments to the claims, Claims 1, 47, 110-124 are allowable.


5. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg  
December 24, 2002

  
W. Gary Jones  
Supervisory Patent Examiner  
Technology Center 1600